

Package leaflet: Information for the user

**Pregnyl 1500 IU, powder and solvent for solution for injection
Pregnyl 5000 IU, powder and solvent for solution for injection**

human chorionic gonadotropin (hCG)

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Pregnyl is and what it is used for
2. What you need to know before you use Pregnyl
3. How to use Pregnyl
4. Possible side effects
5. How to store Pregnyl
6. Contents of the pack and other information

1. What Pregnyl is and what it is used for

Pregnyl contains the hormone known as human chorionic gonadotropin (hCG), which belongs to a group of medicines called gonadotropins. These are important for fertility and reproduction.

Pregnyl is obtained from the urine of pregnant women. HCG has the same effect on the body as luteinising hormone (LH), which is produced in the pituitary gland of men and women. The pituitary is a small hormone-producing gland located at the base of the brain. Together with another pituitary hormone, follicle-stimulating hormone (FSH), LH regulates the function of the reproductive organs (ovaries in women and testicles in men). These hormones are necessary for the normal growth and ripening of egg and sperm cells.

In women

- In women, FSH and LH cause the monthly ripening of an egg cell in one of the ovaries. LH is also needed for ovulation: the release of the egg cell. If the body does not produce enough FSH and LH on its own, this can lead to low fertility. Daily injections of FSH can lead to ripening of the egg cell. Pregnyl ensures that ovulation takes place afterwards.
- Pregnyl can also be given in assisted reproductive techniques, both before and after ovulation.

In men

- In men, Pregnyl can be used on its own or together with an FSH-containing product, when there is underdevelopment of the sex glands or when there are problems with the formation of sperm.

In boys

- In boys, Pregnyl can be used for delayed puberty, on its own or together with an FSH-containing product.
- In some cases Pregnyl can also be given to boys in whom one or both testicles have not descended.

2. What you need to know before you use Pregnyl

Do not use Pregnyl

- if you are allergic to any of the ingredients in this medicine. These are listed in section 6.
- if you have a known or suspected sex hormone-dependent tumour in the ovaries, breast, uterus, prostate, testicles or brain (pituitary or hypothalamus).
- if your reproductive glands (ovaries or testicles) are not working, due to so-called 'gonadal failure'.
- if you are a woman and you have malformations of the sex organs that make pregnancy impossible.
- if you are a woman and you have uterine fibroids (myomas), which make pregnancy impossible.
- if you are a woman and you have heavy or irregular vaginal bleeding, other than menstrual bleeding without a diagnosed cause
- if you are a woman and you have ovarian cysts or enlarged ovaries, not related to Polycystic Ovary Syndrome (PCOS, a condition in which the egg cells do not ripen and no ovulation takes place).

Warnings and precautions

Talk to your doctor or pharmacist before using this medicine.

For men and women:

Please inform your doctor if you:

- have uncontrolled pituitary gland or hypothalamic problems.
- have an underactive thyroid gland (hypothyroidism).
- have adrenal glands that are not working properly (adrenocortical insufficiency).
- have high prolactin levels in the blood (hyperprolactinemia).
- have any other medical conditions (for example, diabetes, heart disease, or any other long-term disease).

Allergic reactions

Allergic reactions, both generalized and local, including swelling of the face, lips, tongue, and/or throat that may cause difficulty in breathing or swallowing (angioedema and anaphylaxis) have been reported. If you have an allergic reaction, stop taking Pregnyl and seek immediate medical assistance. (See also Section 4 Possible side effects).

Misuse for weight control

Pregnyl must not be used for weight loss. HCG has no effect on fat metabolism (burning fat), distribution of fat or appetite.

Chance of having ovarian hyperstimulation syndrome (OHSS)

Treatment with gonadotropic hormones like Pregnyl may cause **ovarian hyperstimulation syndrome (OHSS)**. This is a serious medical condition where the ovaries are overly stimulated and the growing follicles become larger than normal. In rare cases, severe OHSS may be life-threatening. Therefore, close supervision by your doctor is very important. To check the effects of treatment, your doctor will do ultrasound scans of your ovaries. Your doctor may also check blood hormone levels. (See also Section 4 Possible side effects).

OHSS causes fluid to build up suddenly in your stomach and chest areas and can cause blood clots to form. Call your doctor right away if you have:

- severe abdominal swelling and pain in the stomach area (abdomen)
- feeling sick (nausea)
- vomiting
- sudden weight gain due to fluid build-up
- diarrhea

- decreased urine output
- trouble breathing

Ovarian Torsion

Ovarian torsion is the twisting of an ovary. Twisting of the ovary could cause the blood flow to the ovary to be cut off.

Before starting to use this medicine, it is important to inform your doctor if you:

- have ever had ovarian hyperstimulation syndrome OHSS
- are pregnant or think that you may be pregnant
- have ever had stomach (abdominal) surgery
- have ever had a twisting of an ovary
- have past or current cysts in your ovary or ovaries

Chance of having multiple births or birth defects

In pregnancies occurring after treatment with gonadotropic preparations, there is an increased risk of having twins or multiple pregnancies. Multiple pregnancies carry an increased health risk for both the mother and her babies during pregnancy and around the time of birth. Furthermore, multiple pregnancies and characteristics of the patients undergoing fertility treatment (e.g. age of the female, sperm characteristics) may be associated with an increased risk of congenital anomalies.

Chance of having pregnancy complications

In women undergoing fertility treatment there is a slightly increased risk of a pregnancy outside of the uterus (an ectopic pregnancy). Therefore, your doctor should perform an early ultrasound examination to exclude the possibility of pregnancy outside the uterus.

Miscarriage

In women undergoing fertility treatment there may be a slightly higher risk of miscarriage.

Chance of having a blood clot (thrombosis)

Treatment with Pregnyl (like pregnancy itself) may increase the risk of the formation of a blood clot in a blood vessel (thrombosis), most often in the veins of the legs or the lungs.

Blood clots can lead to serious medical conditions, such as:

- blockage in your lungs (pulmonary embolus)
- stroke
- heart attack
- blood vessel problems (thrombophlebitis)
- reduced blood flow to the vital organs that may result in organ damage
- reduced blood flow to your arm or leg that may result in a loss of your arm or leg

Please discuss this with your doctor, before starting treatment, especially if:

- you already know you have an increased risk of blood clots
- you, or anyone in your immediate family, have ever had a blood clot
- you are severely overweight

For up to 10 days after administration of Pregnyl, a pregnancy test may give a false-positive result.

If you are a man:

Antibody formation

If the treatment with Pregnyl is not working, consult with your doctor who may perform additional tests.

Treatment with Pregnyl (hCG) can cause the body to produce substances that act against hCG (antibodies to hCG). In rare cases this could result in ineffective treatment.

Androgen production

Treatment with hCG leads to increased androgen (male sexual hormone) production. Therefore extra supervision by the doctor is necessary

- in the treatment of boys who have not reached puberty. This is because Pregnyl can cause early sexual development and delay growth.
- if you have or have ever had:
 - heart or blood vessel disease
 - kidney disease
 - epilepsy
 - migraine headaches

because worsening or recurrence may occasionally be induced as a result of increased production of androgens (male sexual hormones).

Using other medicines

Interactions of Pregnyl with other medicines have not been investigated; interactions with commonly used medicines can therefore not be excluded.

Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

For up to ten days after administration, Pregnyl may result in a false positive pregnancy test.

Pregnancy and breast-feeding

You must not use Pregnyl during pregnancy. Pregnyl may be used to support a (possible) pregnancy during the period just after ovulation (luteal phase).

If you are breast-feeding, ask your doctor for advice before taking this medicine. Use of Pregnyl can be considered while nursing a baby.

Driving and using machines

As far as is known, Pregnyl has no effect on the ability to drive or operate machines.

Pregnyl contains sodium

This medicine contains less than 1 mmol of sodium (23 mg) per injection, i.e. essentially 'sodium-free'.

3. How to use Pregnyl

Dosage

Always use this medicine exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure. Your doctor will decide on the dose of Pregnyl to be given and will supervise your first injection.

In **female patients** one injection is usually given to induce ovulation and up to 3 injections to support the luteal phase that follows.

In **male patients** (men and boys) the injections are given 2 or 3 times a week. The treatment will last from a few weeks to at least 3 months, depending on the problem being treated. The length of treatment depends on the time needed for development of sperm and the period in which an improvement can be expected.

How the injections are given

The powder for injection from the one vial must be dissolved with the liquid from the other vial (the solvent). This solution must be used immediately after that. The Pregnyl solution can be injected slowly into muscles (for instance, in the buttock [see **Figure 1**], the upper leg or the upper arm) or just under the

skin (for instance, in the lower abdomen [see **Figures 2 and 3**]).

When injecting into a muscle, the injection must be given by the doctor or nurse.

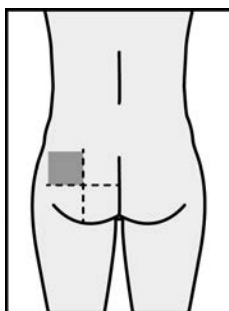


Figure 1

When given under the skin (see **Figures 2 and 3**), injections may, in some cases, be given by yourself or your partner. Your doctor will tell you when and how to do this. If you are injecting yourself with Pregnyl, follow accurately the instructions in the section '**Instructions for use**', so that you administer Pregnyl properly and with minimal discomfort from the injection.

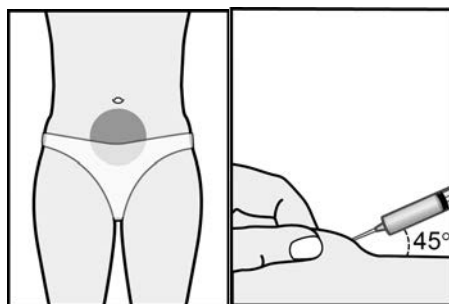


Figure 2

Figure 3

Instructions for use

Step 1 – Getting ready

- Remove the vials of powder and solvent from the refrigerator.
- For the injection, you will need a clean dry surface, alcohol, cotton balls, and a puncture-proof container (sharps bin) to throw away the used syringe and needles.
- Wash your hands and dry them.

Step 2 – Preparing the injection syringe

- Flip off the protective top of the vial of dry powder and of the vial of solvent. **Do not remove the rubber stopper.**
- Wipe the tops of the rubber stoppers with an alcohol wipe.
- Use a syringe and needle that has been recommended by your healthcare provider.
- Attach a needle to the syringe.
- Carefully remove the needle cover (cap) from the needle (See **Figure 4**).



Figure 4

- The dry powder in the glass vial must be dissolved in the solvent from the other glass vial.
- Pierce the needle through the rubber stopper of the solvent vial (see **Figure 5**).



Figure 5

- Draw all the solvent up into the syringe (see **Figure 6**).

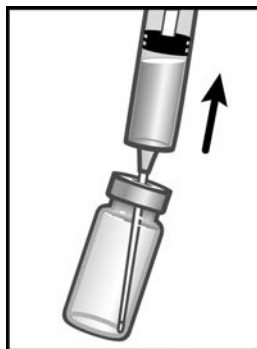


Figure 6

- Inject all the solvent into the vial with the dry powder (see **Figure 7**).

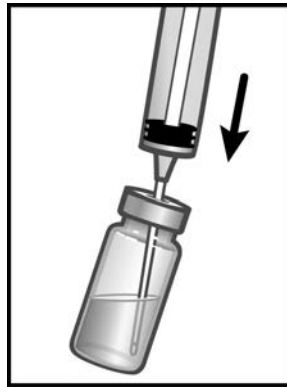


Figure 7

- Remove the syringe and needle from the vial.
- **DO NOT SHAKE OR TURN THE VIAL UPSIDE DOWN**, but swirl gently until the solution is clear. Pregnyl usually dissolves immediately.
- The prepared solution should not be used if it contains particles or is cloudy.
- The solution should be used immediately after reconstitution.
- Make sure that everything is carried out so that during reconstitution sterile conditions are maintained (e.g., never put the syringe down without first putting the protective cap on the needle).
- Draw all of the Pregnyl solution up into the same empty syringe (see **Figure 8**).

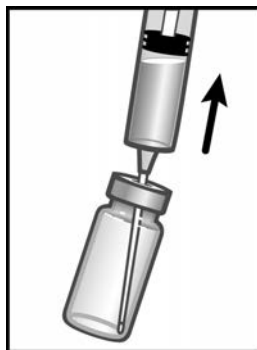


Figure 8

- Replace the longer needle used for drawing up the solution with a shorter sterile injection needle (see **Figure 9**).

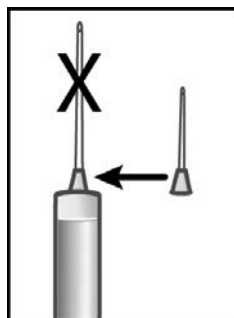


Figure 9

- Hold the syringe with the needle pointing upwards and gently tap the side to allow any air bubbles to rise to the top (see **Figure 10**).

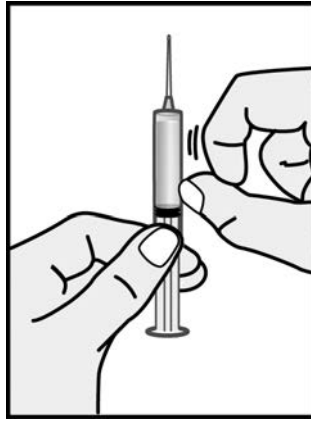


Figure 10

- Then, push the plunger until all the air is out of the syringe and only Pregnyl solution is present in the syringe and the needle (see **Figure 11**).

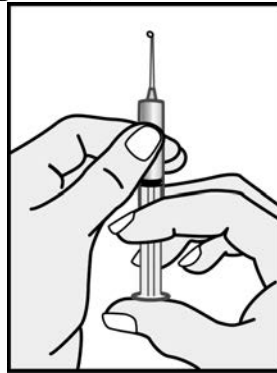


Figure 11

Step 3 – The injection site

The best injection site for subcutaneous injection is in the abdomen around the navel (see **Figure 2**), where there is a lot of loose skin and layers of fatty tissue. Other injection sites are also possible. Choose a slightly different place for each injection. Your doctor or nurse will tell you where to inject.

Step 4 - Preparing the injection site

Tap a few times on the injection site to stimulate tiny nerve endings. This reduces the pain when the needle goes into the subcutaneous tissue. Wash your hands and clean the injection site with alcohol to remove any surface bacteria. Clean an area of about five centimetres (two inches) around the injection site and let the alcohol dry for at least one minute before you go on to the next step.

Step 5 - Inserting the needle

Grasp a fold of skin between thumb and forefinger. With the other hand, stick the needle into the fold of skin at a 45-degree angle, as shown in **Figure 3**.

Step 6 - Checking the correct needle position

Pull the plunger of the syringe back gently, to check that the needle is in the correct position. If blood is drawn into the syringe, it means a vein has been punctured. If this happens, remove the needle from the skin and apply pressure on the injection site with cotton-wool containing alcohol; bleeding should stop after about two minutes. Do not use the solution contaminated with blood. **Start again from step 1** using a new syringe, new needles, and new vials of Pregnyl and solvent.

Step 7 - Injecting the solution

Depress the plunger **slowly** and steadily. This way the solution will be injected properly without injuring subcutaneous tissue.

Step 8 - Removing the syringe

With a quick movement, pull the needle out of the skin and apply pressure on the injection site with cotton-wool containing alcohol. Gently massaging the skin – while you are still applying pressure – helps disperse the Pregnyl solution more easily and reduces the pain. Any remaining solution should be discarded. Do not mix Pregnyl with any other medicines.

Step 9 – Disposing the needles

In order to prevent injury, do not put the syringe back into the protective sheath. Carefully dispose of all the needles you used. You can either dispose of needles in a sharps bin or take them to your pharmacy to be destroyed. Do not share your needles or syringes with others.

If you use more Pregnyl than you should

If you used too much Pregnyl, contact your doctor or pharmacist immediately. The toxicity of Pregnyl is very low, but a dose of Pregnyl that is too high can cause ovarian hyperstimulation syndrome (see also section 2, ‘Warnings and precautions’ and section 4 on ‘Possible side effects’).

If you forget to use Pregnyl

Never take a double dose to make up for a forgotten dose. Tell your doctor that you missed a dose.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. Most of these reactions are of a mild nature and go away on their own. Common side effects occur in less than 1 in 10 patients. Uncommon side effects occur in less than 1 in 100 patients. Rare side effects occur in less than 1 in 1000 patients.

Pregnyl can cause bruising, pain, redness, swelling and itching at the site of injection. Allergic reactions are rare, and mostly involve pain or rash at the injection site. In rare cases generalized hypersensitivity can occur, such as a rash on several areas of the body, or fever (see section 2 Warnings and precautions).

If you are a woman

A possible complication of treatment with gonadotropic hormones like Pregnyl is unwanted overstimulation of the ovaries. The chance of having this complication can be reduced by carefully monitoring the number of maturing follicles (small round sacs in your ovaries that contain the eggs). Your doctor will do ultrasound scans of your ovaries to carefully monitor the number of maturing follicles. Your doctor may also check blood hormone levels. The first symptoms of ovarian overstimulation may be noticed as pain in the stomach (abdomen), feeling sick or diarrhea. Ovarian overstimulation may develop into a medical condition called ovarian hyperstimulation syndrome (OHSS), which can be a serious medical problem. In more severe cases this may lead to enlargement of the ovaries, collection of fluid in the abdomen and/or chest (which may cause sudden weight gain due to fluid build-up) or clots in the blood vessels (See also Section 2 Warnings and precautions). Contact your doctor without delay if you have pain in the stomach (abdomen) or any of the other symptoms of ovarian hyperstimulation, even if they occur some days after the administration of Pregnyl has been given. Rarely, blood clots may occur without unwanted overstimulation of the ovaries (see also section 2. Before you use Pregnyl).

If you are a man

In men, fluid and salt may be retained in the tissues, marked usually by swelling of the ankles or feet and, in rare cases, enlargement of the breasts. This may be caused by increased androgen production due to treatment with hCG. If any of these symptoms appear, tell your doctor immediately.

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via Netherlands Pharmacovigilance Centre Lareb, website www.lareb.nl. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Pregnyl

Keep this medicine out of the sight and reach of children.
Store in the original package in order to protect from light.
Store in the dark at 2 – 8 °C (in a refrigerator).

The solution should be used immediately after reconstitution.

Do not use this medicine after the expiry date which is stated on the package after 'EXP'. There you will see a month and a year. The expiry date is the last date of that month.

Do not use Pregnyl if you notice that the reconstituted solution contains particles or if the solution is not clear.

Medicines should not be flushed down the drain or the toilet, and do not dispose of them with household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will ensure that they are disposed of responsibly and do not end up in the environment.

6. Contents of the pack and other information

What Pregnyl contains

- The active ingredient is human chorionic gonadotropin (hCG), in doses of 1500 IU or 5000 IU per vial.
- The other ingredients of this medicine are mannitol, disodium hydrogen phosphate, sodium dihydrogen phosphate and sodium carboxymethylcellulose. The solvent contains sodium chloride (9 mg) and water for injection (1.0 ml).

What Pregnyl looks like and contents of the pack

One glassvial contains a white dry powder or cake. This powder or cake is reconstituted with the solvent from the other glass vial. The solvent is a clear, colourless watery solution.

Pregnyl 1500

- One pack contains 3 vials of 2 ml with powder for injection, equivalent to 1500 IU hCG, and 3 vials that contain 1 ml of solvent.

Pregnyl 5000

- One pack contains 1 or 3 vials of 2 ml with powder for injection, equivalent to 5000 IU hCG, and 1 or 3 vials that each contain 1 ml of solvent.

Not all pack sizes listed may be available on the market.

Marketing Authorisation Holder and Manufacturer

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